Remarks

Claims 1, 3-12, 25 and 28 are pending. Claims 1, 3, 4, 5, 8, 9, 10, 11, 12, 25 and 28 have been amended. Claims 2, 13-24, 26, 27 and 29-41 have been cancelled. Amendment to the claims can be found throughout the specification.

35 U.S.C. 112, second paragraph rejection

Claims 14, 15, 18, 19, 21 and 24-26 have been canceled from the present set of claims. Therefore, Applicants respectfully request the 35 U.S.C. 112, second paragraph rejections be withdrawn from consideration.

35 U.S.C. 103(a) Rejection

Claims 1-41 were rejected under 35 U.S.C. 103(a) as being unpatentable over O'Reilly et al. in view of Williams et al. (Cochrane Reviews 2002). The Examiner argues that it would have been obvious to a person of ordinary skill in the art at the time of applicant's invention to administer the epothilone of O'Reilly in a daily continuous intravenous administration lasting 6-24 hours, since an adjustment to the time of infusion treatment is simply routine optimization. The Examiner also argues that it would have been obvious to a person of ordinary skill in the art at the time of applicant's invention to adjust the infusion time of O'Reilly to 6-24 hours since Williams suggest that a compound (pacilatexl or taxol), which mimics the biological effects had has the same binding site of epothilone, administered at a 24 hour infusion, may be more efficacious compared to a shorter infusion of 3 hours. Applicants respectfully disagree.

The present set of claims define methods of treating patients suffering from colorectal cancer comprising administering an effective amount of epothilone B over 1 to 14 days, together with a pharmaceutically acceptable carrier, wherein the daily administration is by continuous intravenous administration lasting 6 to 24 hours, please refer to amended claim 1. The present invention covers a clinical trial, recently completed by Novartis, which describes epothilone B in a Phase I 6-arm trial to optimize administration exploring single dose bolus and continuous infusion over 1 or 5 days every 3 or 4 weeks in patients with pretreated advanced colon cancer with nutritional support treatment and intensive medical management of diarrhea. One of the side effects clinically observed with the use of EPO906 is severe diarrhea, grade 1- grade 3. Grade 3 diarrhea can be life threatening. Therefore, it was important to the inventors to establish a proper dosing schedule to optimize the clinical effects of EPO906 while reducing the side effect of diarrhea, please refer to page 34 second to last bullet point in the specification.

None of the references cited provide the necessary motivation to combine the references to arrive at the claimed invention, *In re Rouffet,* 149 F.3d 1350, 1357, 47 USPQ2d 1453, 1457-58 (Fed. Cir. 1998). O'Reilly, also assigned to Novartis, describes intravenous infusion of epothilone B or A once every three weeks to adult patients with advanced solid tumors who have failed

standard systemic therapy or for whom standard systemic therapy does not exist, see col. 47, lines 43-48. As properly stated by the Examiner, O'Reilly does not teach a daily continuous intravenous administration lasting 6 to 24 hours. The focus of O'Reilly was establishing a dose that would be used to treat patients individually. For example, the dose would allow for treatment of a disease if the dose was calculated according to the following formula (I)
Single dose (mg/m^2)=(0.1 to y)xN

At the time of O'Reilly, it would not have been obvious to a person of ordinary skill in the art to modify the calculated dose as described in O'Reilly so that the administration would be continuous for 6 to 24 hours because it was not known at the time of O'Reilly that EPO906 may have side effects associated dosing. The level of skill in the art, at the time of the invention, cannot be relied upon to provide the suggestion to combine references. *Al-Site Corp. v. VSI Int'l Inc.*, 174 F.3d 1308, 50 USPQ2d 1161 (Fed. Cir. 1999). More specifically, the knowledge of side effects associated with EPO906, including diaraheia, which was used to develop the continous dosing schedule of the present invention cannot be applied to O'Reilly to modify the dosing schedule described in O'Reilly.

Williams et al. state that three hour paclitaxel infusions appear to result in a small fall in white blood cell count, less fever, infection and sore mouth than compared to the 24 hour infusions. Epothilone B is not described in the Williams et al. article. Although the Examiner argues that paclitaxel mimics the biological effects and has the same binding site of epothilone and therefore it would have been obvious to expect similar success, Applicants believe this line of argument is illogical. Paclitaxel and Epothilone B are two different therapeutic agents, with different chemical structures. The dosing regimen to avoid a specific set of side effects of paclitaxel cannot be applied to epothilone B. Furthermore, there is no suggestion in the Williams et al. article that the new dosing schedule for paclitaxel would be applicable to other therapeutic agents. Therefore, the claimed invention is non-obvious over the cited references because the references to do not teach or suggest or provide the requisite motivation for a person of ordinary skill in the art to make the claimed invention. Applicants respectfully request the obviousness rejection be withdrawn from consideration. Entry of this Response is respectfully requested.

Respectfully submitted,

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